REMARKS/ARGUMENTS

I. Status of the Claims

After entry of this amendment, claims 1-23 and 25-29 are pending in this application. Claim 24 is herein canceled, and claims 1, 8, 17, 20, 25 and 26 are herein amended.

Applicant brings to the Examiner's attention that she has not addressed the status of claims 27-29, which were added in the previous amendment filed April 4, 2005.

Claims 1, 17 and 20 have been amended to delete the possibility of SEQ ID NO:2.

Claim 1 has been further amended to replace "selected from among members of the DVR family including the TGF-β superfamily" with "a bone morphogenetic protein (BMP) or a growth differentiation factor (GDF)." This amendment is supported in original claim 1 and in the specification, *e.g.*, at page 2, lines 23 to 29, and at page 14, lines 8-11, because members of the BMP and GDF families are members of the TGF-β superfamily.

Claim 8 has been amended to include "GDF-5" as a possibility for a polypeptide variant. This amendment is supported in the specification, *e.g.*, at page 3, lines 11-14, and page 20, lines 9-13 and 22-23.

Claim 25 has been amended to delete "for osteoinduction", which merely removes the therapeutic purpose for the claimed composition.

Claim 26 has been amended to delete "An osteoinductive" and add "A", which merely removes the therapeutic purpose for the claimed matrix.

No new matter is added by the foregoing amendments.

III. Objection to Claims 1, 2, 4-9 and 11-26 as Encompassing Non-Elected Subject Matter

The objection to claims 1, 2, 4-9 and 11-26 as encompassing non-elected subject matter has been maintained because the restriction requirement of June 1, 2004 has been maintained. Applicant has amended claims 1, 17 and 20 to delete SEQ ID NO:2 from the claims, thereby rendering moot this ground of objection.

IV. Rejection of Claims 1, 2, 4-7, 9 and 11-26 under 35 U.S.C. § 102

The rejection of claims 1, 2, 4-7, 9 and 11-26 as being anticipated by U.S. Application publication number 2001/0020086 (the '086 application) has been maintained for reasons of record in the Office Action of September 29, 2004. The Examiner alleges that the sequence CRKRCN, which is disclosed in the '086 application, comprises SEQ ID NO:1 and therefore anticipates Applicant's claims to SEQ ID NO:1. Applicant respectfully traverses this rejection as it may be applied to amended claims 1 and 17, and claims dependent therefrom.

The '086 application fails to anticipate amended claims 1 and 17, and claims dependent therefrom, because the cited reference fails to teach every element of the currently claimed invention. The heparin-binding domain disclosed in the '086 application, whether it is properly determined to be CRKNRCN or CRKRCN as alleged by the Examiner (see below), is an integral part of a larger protein, human lipoprotein lipase (LPL). The '086 application discusses addition of such heparin-binding domains to proteins that do not have a native heparin-binding domain (see, for examples, paragraphs 4 and 78). In contrast, in the instant application, the oligopeptides of SEQ ID NO:1 are added to, inserted into, and/or substituted into polypeptides that contain heparin-binding domains, namely, members of the bone morphogenetic protein (BMP) and growth differentiation factor (GDF) families. There is no teaching in the '086 application that the human LPL heparin-binding domain is added to, inserted into, and/or substituted into polypeptides that already contain a heparin-binding domain. As such, the '086 application fails to anticipate the claimed invention.

Applicant further notes that the sequence CRKRCN alleged to be disclosed by the Examiner is an obvious typographic error. In this case, Table 1 of the '086 application discloses two heparin-binding domain sequences from human LPL: AKRSSKM and CRKRCN; however, the literature reference cited for these sequences makes clear that the latter heparin-binding domain sequence is actually CRKNRCN, not CRKRCN (see Hata et al., *J. Biol. Chem.* 268-8447-8457, 1993, copy attached). A person skilled in the art would not have ignored such a clear reference to Hata, and upon reviewing this reference would have immediately recognized that the correct sequence of one of the human LPL heparin-binding domains is CRKNRCN, not CRKRCN. The Hata reference provides experimental data showing that CRKNCRN is a heparin-binding domain. In contrast, neither the Hata reference nor the '086 application show CRKRCN to be a heparin-binding domain. Clearly, the disclosure of CRKRCN in the '086 application was accidental, and not deliberate or a necessary consequence of what was intended. Because the purpose of Table 1 in the '086 application was to disclose known heparin-binding domains, the disclosure of CRKRCN, which was not known previously as a heparin-binding domain, could not have been intended. Accordingly, Applicant respectfully submits that assuming *arguendo* a skilled person were to have attempted to modify the teaching of the cited reference he would have done so starting from the correct sequence CRKNRCN rather than the typographic error CRKRCN.

Because the '086 application does not teach that the human LPL heparin-binding domain is added to, inserted into, and/or substituted into a polypeptide that already contains a heparin-binding domain, Applicant respectfully requests that the rejection of claims 1, 2, 4-7, 9 and 11-26 as being anticipated by the '086 application be withdrawn.

V. Rejection of Claims 1, 2, 4-7, 9 and 11-26 under 35 U.S.C. § 103

The rejection of claims 1, 2, 4-7, 9 and 11-26 as being unpatentable over the '086 application in view of U.S. Patent No. 5,652,332 (the '332 patent) was maintained for reasons of record in the Office Action of September 29, 2004. The Examiner alleges that the sequences disclosed in the '332 patent anticipates Applicant's SEQ ID NO:1. Applicant respectfully

traverses this rejection as it may be applied to amended claims 1 and 17, and claims dependent therefrom.

The peptides disclosed in the '332 patent are biologically active, functional domains of the bacteriocidal/permeability-increasing protein (BPI) that are able to bind to heparin and/or neutralize heparin. Two of these peptides, BPI.2 and BPI.3, contain the sub-sequence, KRFL, which allegedly satisfies the requirements of SEQ ID NO:1 in amended claim 1. Unlike the '332 patent, however, the polypeptide variant of amended claim 1 comprises an oligopeptide(s) of SEQ ID NO:1 that is added to, inserted into, and/or substituted into a polypeptide that is a member of the BMP or GDF family. Because human BPI is not a member of either the BMP or GDF family, the '332 patent fails to anticipate the currently claimed invention.

There was no motivation for a person skilled in the art to combine a targeted selection of one or two heparin-binding fragments from the many fragments disclosed in the '332 patent with the teaching of growth factors with added heparin-binding domains disclosed in the '086 application. The '332 patent discusses two peptides, BPI.2 (IKISGKWKAQKRFLK) and BPI.3 (NVGLKFSISNANIKISGKWKAQKRFLK), containing the amino acid sub-sequence KRFL, which allegedly satisfy the requirements of Applicant's SEQ ID NO:1 (X_1 is K; X_2 is R; X_3 is nothing; X_4 is not K, R or H; X_5 is nothing; and X_6 is not K, R or H). There was no teaching, suggestion, or motivation in the '332 patent to select the peptide sequence KRFL from BPI.2 and BPI.3 as the heparin-binding domain to be added to a growth factor as taught by the '086 application for the following reasons. First, the '332 patent teaches that BPI.2 has little or no heparin-binding activity, and BPI.3 has only moderate heparin binding activity (see Figure 6 in Example 10). Second, the '332 patent teaches that alanine substitution at most of the amino acid positions in BPI.2 results in decreased heparin-binding affinity and heparin-binding capacity (see Table V in Example 18). Third, the '332 patent discloses more than 220 BPI peptide sequences, many of which have some heparin-binding activity. Based on these results, a person skilled in the art would have no basis for choosing the KRFL peptide, which is a short, partial sequence of 4 amino acids present in both of the BPI.2 and BPI.3 fragments as the heparin-

binding domain to be added to a heterologous protein. Fourth, as discussed above, the '086 application discusses adding a heparin-binding domain to growth factors that do not have a native heparin-binding domain, and there is no teaching, suggestion, or motivation in the '086 application to add heparin-binding domains to growth factors that already have native heparin-binding domains. The '332 patent does not compensate for the deficiency of the '086 application and does not provide any teaching, suggestion, or motivation to add heparin-binding domains to members of the BMP or GDF families, which already have native heparin-binding domains. Finally, the targeted selection of the BPI peptide KRFL cited by the Examiner appears to be based on hindsight-directed analysis and the desire to arrive at the features of claim 1 from any available prior art document. The Examiner has not set forth any objective evidence why a person skilled in the art would choose this particular peptide to arrive at the claimed invention. In light of the foregoing, Applicant respectfully requests that the rejection of claims 1, 2, 4-7, 9 and 11 as being unpatentable over the '086 application in view of the '332 patent be withdrawn.

The rejection of claim 8 as being unpatentable over the '086 application in view of Linkhart et al. (the Linkhart reference) was maintained for reasons of record in the Office Action of September 29, 2004. The Examiner alleges that it would have been obvious to one of ordinary skill in the art to combine the teachings to modify BMPs with heparin-binding sites so that they can be used with matrices like heparin and fibrin. Applicant respectfully traverses this rejection as it may be applied to amended claim 1 and claims dependent therefrom, including amended claim 8.

Amended claim 8 depends from claim 1 and is non-obvious for at least the same reasons as discussed above for claims 1, 2, 4-7, 9, and 11-26. In addition, there was no motivation to combine the teachings of the '086 application and the Linkhart reference. The Linkhart reference discusses modifying BMPs to bind to specific sites in bone. The heparin-binding domains discussed in the '086 application would be expected to increase binding of a polypeptide to heparin, but there is no teaching in the '086 application that heparin-binding domains confer binding to bone in a site-specific manner. Instead, the '086 application teaches

that heparin-binding domains are found on a variety of proteins that do not bind to specific sites in bone. Thus, one skilled in the art interested in modifying BMP or GDF family members to bind to specific sites in bone would have had no reason to add heparin-binding domains, because such addition would have been expected to increase heparin-binding ability regardless of the location of the heparin. The Linkhart reference does not compensate for the deficiency of the '086 application and does not provide any teaching or suggestion that adding a heparin-binding domain to a BMP would increase its binding to bone at specific sites. Thus, amended claim 8 is non-obvious over the '086 application and the Linkhart reference. Accordingly, Applicant respectfully requests that the rejection of claim 8 as being unpatentable over the '086 application in view of the Linkhart reference be withdrawn.

VI. Rejection of Claims 1, 2, 4-9 and 11-26 under 35 U.S.C. § 112, First Paragraph

A. Enablement

The rejection of claims 1, 2, 4-9 and 11-26 as lacking enablement was maintained for reasons of record in the Office Action of September 29, 2004. The Examiner alleges that by Applicant's own assertion SEQ ID NO:1 does not describe the essential features of heparin-binding peptides and, thus, it would require undue experimentation to use members of the claimed genus, and it is not predictable that the heparin-binding peptides will have no effect on protein function.

As an initial matter, there appear to be several misunderstandings in the Final Office Action. First, the Examiner mistakenly states that "while Applicant asserts that three positively charged residues are required for heparin binding, Applicant's generic sequence only requires two. Thus, according to Applicant, the essential features of heparin binding are not required by SEQ ID NO:1." The response filed April 4, 2005 states that, for SEQ ID NOs:1 and 2, X_1-X_3 comprise at least two positively charged (basic) amino acids (see pages 10 and 20) and at least 2 out of 3 are basic amino acids (see page17). As such, there is no discrepancy between

the essential features for the heparin-binding motifs of the presently claimed invention and SEQ ID NO:1.

Second, the Examiner mistakenly alleges that the structural motif of SEQ ID NO:1 requires only 4 amino acids, of which 2 can vary among 3 amino acids and the other 2 among 17 amino acids. In fact, the motif may consist of only 3 amino acids (when X_3, X_5 and X_6 are no amino acid). Thus, the motif comprises 2 or 3 basic (K, R or H), and at least 1 non-basic (not K, R or H) amino acid. In the case of further amino acids, at least 1 or 2 non-basic amino acids are added to the C-terminal end of the motif. Consequently, the structural motif has a specific charge distribution of 2 to 3 positively charged (basic) amino acids, followed by 1 to 3 non-positively charged (non-basic) amino acids. This positively charged motif is complementary to negatively charged heparin or heparin-like substances.

Third, the Examiner notes that heparin-binding domains or motifs disclosed in the '086 application and '332 patent are not encompassed by SEQ ID NO:1 and, for this reason, the sequence of the invention does not provide all of the features necessary for heparin binding. The Examiner's logic here is flawed because the features of the heparin-binding motif claimed by the Applicant need not, nor are they meant to, encompass each and every heparin-binding domain. It is up to the Applicant to select the scope of the desired patent protection. That there may exist heparin-binding motifs that fall outside the scope of SEQ ID NO:1 is irrelevant to the issue of whether the instant claims are enabled.

The Examiner alleges that "it would require undue experimentation for the artisan to use members of the genus Applicant has claimed, regardless of the simplicity of making and assaying such members, because the number of encompassed polypeptides is very large and the essential features of heparin binding are not described, and the artisan would not be able predict which members of this large genus would actually have the desired activity." Applicant respectfully disagrees for the following reasons.

First, as *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), makes clear, the issue for enablement is not whether any experimentation is needed, but whether the experimentation needed is undue. The Examiner has not alleged that the experiments needed to determine whether an oligopeptide encompassed by SEQ ID NO:1 increases heparin-binding ability to a heterologous polypeptide require anything other than routine experimentation. In fact, the Examiner acknowledged the simplicity of making and assaying members of the genus. As such, even if the number of encompassed polypeptides is very large, mere routine experimentation would be required to determine if any oligopeptide satisfying the requirements of SEQ ID NO:1 confers the desired activity. The previous response, dated April 4, 2005, outlines the routine steps disclosed in the specification that would allow one skilled in the art to screen a reasonable number of polypeptide variants for increased heparin-binding ability.

Second, contrary to the Examiner's allegation, the essential features of the heparin binding oligopeptides of SEQ ID NO:1 are described. One skilled in the art would recognize that the essential features of the structural motif of SEQ ID NO:1 are: (1) a specific charge distribution of 2 to 3 positively charged (basic) amino acids, (2) followed by 1 to 3 non-positively charged (non-basic) amino acids, (3) wherein the positively charged motif is complementary to the negatively charged heparin or heparin-like substances. Armed with this clear definition of SEQ ID NO:1, one skilled in the art could determine by mere inspection of the amino acid sequence whether any particular oligopeptide has the claimed structural motif.

Third, the Examiner has failed to explain why the skilled artisan could not identify or predictably use members of the genus. Moreover, the Examiner has failed to set forth any objective evidence or reasoning to doubt that an oligopeptide that satisfies the requirements of SEQ ID NO: 1 confers heparin-binding ability to a polypeptide variant of claim 1. Contrary to the Examiner's mere allegation of unpredictability, the disclosure provides sufficient guidance so that one skilled in the art could identify members of the genus and predictably use members of the genus to increase the heparin binding ability of heterologous polypeptides.

As detailed above, one skilled in the art could identify members of the genus satisfying the requirements of SEQ ID NO:1 by mere inspection of the amino acid sequence of the peptide. One skilled in the art would expect oligopeptides of SEQ ID NO:1 to share the heparin-binding of the exemplified species (T3 and T4) because the heparin-binding results from the combination of the charge distribution of the heparin-type substances and charge distribution and arrangement of basic and non-basic amino acids of the exemplified species. The claimed motifs require that its members have the same charge distribution and arrangement of basic and non-basic amino acids as the exemplified species. One skilled in the art would therefore expect the claimed motifs to bind heparin, as do the exemplified sequences.

The test under *In re Wands* is not whether each and every possible variant within the present claims has increased heparin-binding activity but rather whether it is feasible to screen a reasonable number that do without undue experimentation. Here, a reasonable number of variants can be screened for heparin-binding activity by repetition of routine steps. The Examiner has already acknowledged the simplicity of making and assaying members of the genus. There is nothing difficult in making polypeptide variants falling in the scope of claim 1. Armed with the definition of the oligopeptides of SEQ ID NO:1, one would know whether an oligopeptide falls within the scope of the claim 1. The polypeptides of claim 1, members of the BMP or GDF family, are well-known in the art. Mere standard molecular biology techniques are required to make the polypeptide variants of claim 1. There is nothing difficult in testing the polypeptide variants of claim 1 for their ability to bind heparin. The disclosure provides simple heparin-binding assays, which are well-known in the art. Thus, a reasonable number of variants having heparin-binding activity would be obtained by routine molecular biology and a simple *in vitro* assay. As held by *Wands,* practitioners of the art are prepared to undertake this type of screening to identify molecules having a desired property.

The Examiner next alleges that "since the sequences encompassed by the SEQ ID NO:1 are not limited in size and may be, outside of the requirements discussed above, of almost any composition, it is not predictable that they would have no effect on protein function."

Applicant respectfully disagrees with the Examiner's characterization of the oligopeptides of SEQ ID NO:1 and their effect on protein function.

First, contrary to the Examiner's allegation, the sequences encompassed by SEQ ID NO:1 are limited both in size and composition. The heparin binding motif of SEQ ID NO:1 is 3, 4, 5 or 6 amino acids in length, and must have 1 of 3 amino acids (K, R or H) at 2 to 3 positions and 1 of 17 amino acids at 1 to 3 positions. To illustrate these limitations, for a heparin binding motif of 3 amino acids (X_1, X_2, and X_4), 153 of 8000 or about 2% of possible tripeptides fulfill the requirements of SEQ ID NO:1, and for a heparin binding motif of 6 amino acids (X_1-X_6), only 133,651 of 64,000,000 or about 0.2% possible hexapeptides fulfill the requirements of SEQ ID NO:1.

Second, the claimed invention does not require that the addition, insertion, and/or substitution of one or more oligopeptides of SEQ ID NO:1 into a heterologous polypeptide has no effect on function of the resultant polypeptide variants. Rather, the polypeptide variants of amended claim 1 must have increased heparin-binding ability and have at least one biological activity (see definition of "polypeptide" on page 7, lines 1 to 4 of the specification). Applicant respectfully submits that one skilled in the art, armed with the specification and the knowledge of the structure-function relationships of BMP and GDF family members, would be able to add, insert, and/or substitute one or more oligopeptides of SEQ ID NO:1 into a BMP or GDF family member in such a way as to increase heparin-binding ability while retaining, at least to some degree, the biological activity of the unaltered polypeptide.

Furthermore, the Examiner has failed to provide any objective evidence or reasoning to support her allegation that the skilled artisan would not be able to predict which sequences "could be inserted into molecules with no effect on protein function." Other than commenting that the sequences are "so divergent in size and composition", the Examiner has failed to explain why one skilled in the art could not predict which sequences could be added, inserted, and/or substituted into a BMP or GDF member polypeptide and increase heparin-binding ability and retain, at least to some degree, biological activity. As detailed above, the

oligopeptide sequences of SEQ ID NO:1 are not unlimited in size and composition as alleged, and there is sufficient knowledge in the disclosure and in the art to predict where to add, insert, and/or substitute an oligopeptide into a BMP/GDF polypeptide and retain, at least to some degree, biological activity. The Examiner's mere allegation is unsupported by objective evidence or reasoning, and, as stated in the MPEP § 2164.05, page 2100-191, "the Examiner should never make the determination based on personal opinion."

With respect to amended claim 7, the Examiner alleges that the claim "still encompasses all "biological activities"" and that "there is no guidance as to how variants with the same activities as polypeptides claimed can be made and used." As amended, claim 7 requires that at least one oligopeptide satisfying the requirements of SEQ ID NO:1 be added, inserted and/or substituted into a polypeptide of the BMP or GDF family such that the resultant polypeptide variant has increased heparin-binding ability, while retaining at least 10% of the biological activity of, and at least 90% homology to, the unaltered polypeptide. As discussed in the previous response, claims of this type specifying variants of a polypeptide constrained by 90% homology and retention of some biological activity have been routinely granted by the PTO. Moreover, the biological activities of BMP and GDF family members are disclosed in the specification and are well-known in the art. Given this disclosure and the state of knowledge regarding BMP and GDF family members, Applicant respectfully submits that the skilled artisan would recognize where to add, insert, and/or substitute heparin-binding domains into a BMP or GDF polypeptide with the reasonable expectation that the resultant polypeptide variant will satisfy all of the limitations of claim 7 as amended. For the skilled artisan, merely routine experimentation is required to make and use polypeptide variants that satisfy the requirements for increased heparin-binding ability, with at least 10% of the biological activity of, and at least 90% homology to, the respective unaltered BMP or GDF polypeptide.

With respect to claims 24-26, the Examiner alleges that the skilled artisan would not be able to use all members of the DVR family for wound healing because the specification does not teach conferring this activity on a protein that lacks this activity by virtue of increasing the protein's ability to bind heparin.

Applicant has canceled claim 24, thereby rendering moot this ground of rejection.

Applicant has amended claims 25 and 26 to remove the recitation of therapeutic purpose, thereby rendering moot this ground of rejection. Thus, claim 25 is directed to a composition comprising a polypeptide variant of claim 1 and a carrier, and claim 26 is directed to a matrix that contains or is coated by heparin or heparin-like substances, and a polypeptide variant of claim 1 is adsorbed to the heparin or heparin-like substances.

In light of the foregoing, Applicant respectfully requests that the rejection of claims 1, 2, 4-9 and 11-26 as lacking enablement be withdrawn.

B. Written Description

The rejection of claims 1, 2, 4-9 and 11-25 as lacking written description was maintained. The Examiner alleges that the claimed genus is highly variant because the structural requirements are so limited, and that the structural requirement of the claimed genus "is not sufficient to characterize and identify a genus of heparin-binding sequences." Applicant respectfully traverses this rejection.

As an initial matter, there appear to be further misunderstandings in the instant Final Office Action. First, the Examiner states "by Applicant's own admission, three positively charged residues are required." As mentioned above, Applicant's remarks in the response filed April 4, 2005, and maintained herein, state that 2 or 3 positively charged residues are required. Second, the Examiner states that "the cited references teach many heparin-binding factors that do not have even these minimum required characteristics." That other heparin-binding factors do not have the structural motif of SEQ ID NO:1 is irrelevant because Applicant is not claiming polypeptide variants modified to contain any heparin-binding domain, but only those modified to contain at least one oligopeptide that satisfies the requirements of SEQ ID NO:1.

The claimed genus (oligopeptides satisfying the requirements of SEQ ID NO:1) is neither highly variant nor so limited in its structural requirements as the Examiner contends. As

discussed above, the oligopeptides of SEQ ID NO:1 are limited in both size and composition: they must be 3 to 6 amino acids in length, and include 2 or 3 positively charged (basic) amino acids, followed by 1 to 3 non-positively charged (non-basic) amino acids. Thus, the claimed genus is restricted both in size and composition, as well as in the order of basic and non-basic amino acids. This feature of the oligopeptides, where non-basic amino acids follow basic amino acids, provides the key component of the structural requirement of the claimed genus, namely the provision of a positively charged motif that is complementary to the negatively charged heparin or heparin-like substances to which the oligopeptides bind. The claimed genus is not highly variant because, as exemplified above for tri- and hexa-peptides of the invention, only a small percentage of possible peptides satisfy the structural requirements of SEQ ID NO:1. Thus, the claimed genus is also not so limited in its structural requirements because there are restrictions on size, composition, and order of amino acids.

Adequate written description can be provided by description of structural features commonly possessed by members of the claimed genus that distinguishes them from others. *Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398, (Fed. Cir. 1997). Here, the specification and claims describe structural features commonly possessed by the oligopeptides of SEQ ID NO:1, as required by *Lilly*. In particular, the oligopeptides of SEQ ID NO:1 have a common structural motif, namely, the combination of X_1-X_3 and X_4-X_6, wherein X_1-X_3 includes 2 to 3 positively charged (basic) amino acids capable of interacting with the negatively charged sulfated glucosaminoglucanes, and X_4-X_6 includes 1 to 3 non-positively charged (non-basic) amino acids. The fact that heparin-binding domains exist that fall outside the requirements of SEQ ID NO:1 is irrelevant to the issue as to whether members of the claimed genus commonly possess a structural motif, as is the case here.

The Examiner's allegation that the structural requirement of the claimed genus "is not sufficient to characterize and identify a genus of heparin-binding sequences" is not supported by any objective evidence or adequate reasoning. In the absence of any such objective evidence or adequate reasoning, Applicant respectfully submits that the structural requirements of SEQ ID NO:1, as described in detail above, are indeed sufficient to characterize and identify a genus of

heparin-binding sequences. Accordingly, Applicant respectfully requests that the rejection of claims 1, 2, 4-9 and 11-25 as lacking written description be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

Neil G. Miyamoto
Reg. No. 50,370

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 650-326-2400
Fax: 415-576-0300
Attachments
NGM:ngm
60611323 v1